FIG. 1

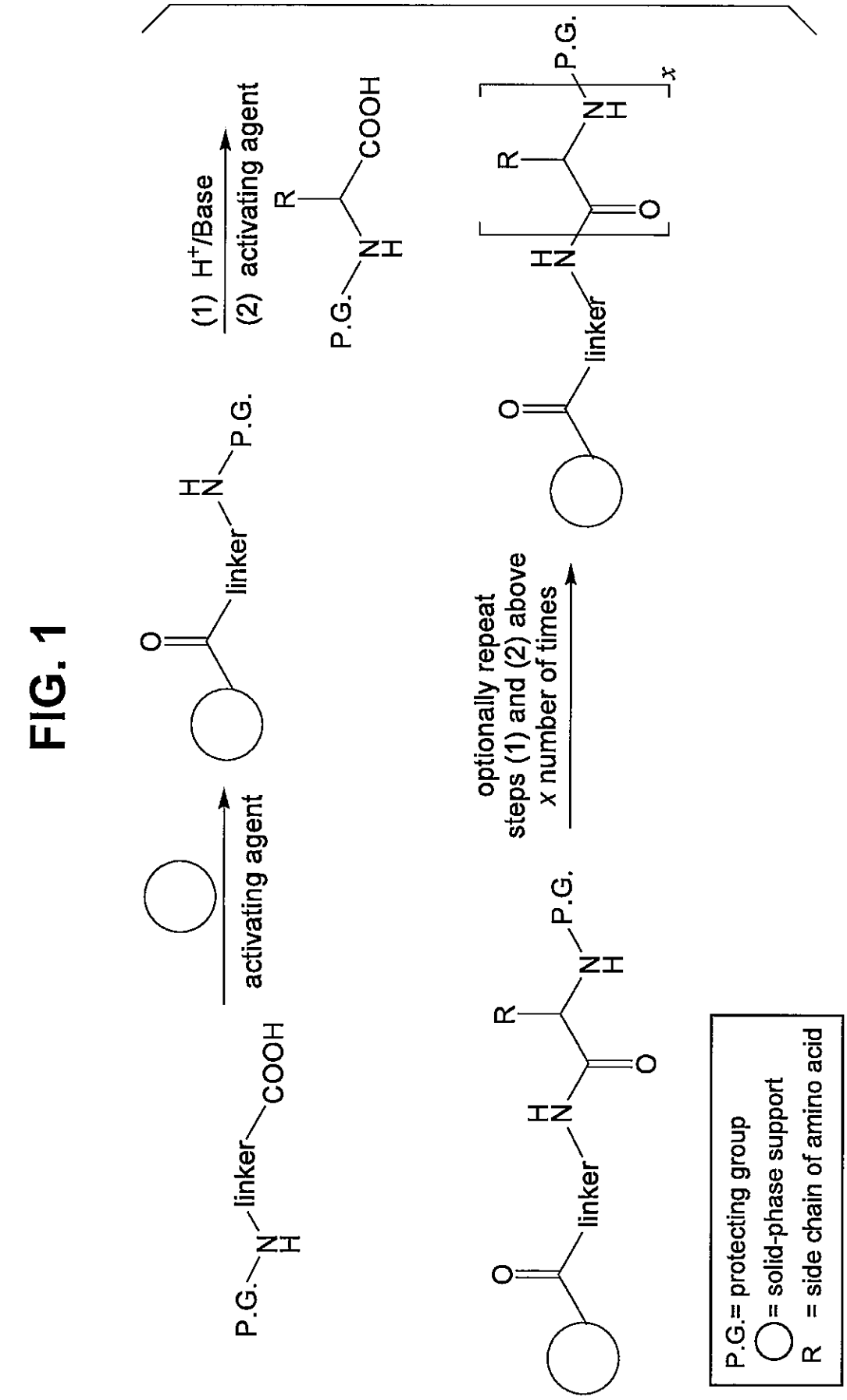

P.G.
NH
linker
COOH
activating agent
O
linker
NH
P.G.
(1) H+/Base
(2) activating agent
R
COOH
NH
P.G.
optionally repeat
steps (1) and (2) above
x number of times
P.G.
NH
R
O
x
P.G.= protecting group
= solid-phase support
R = side chain of amino acid

FIG. 1B

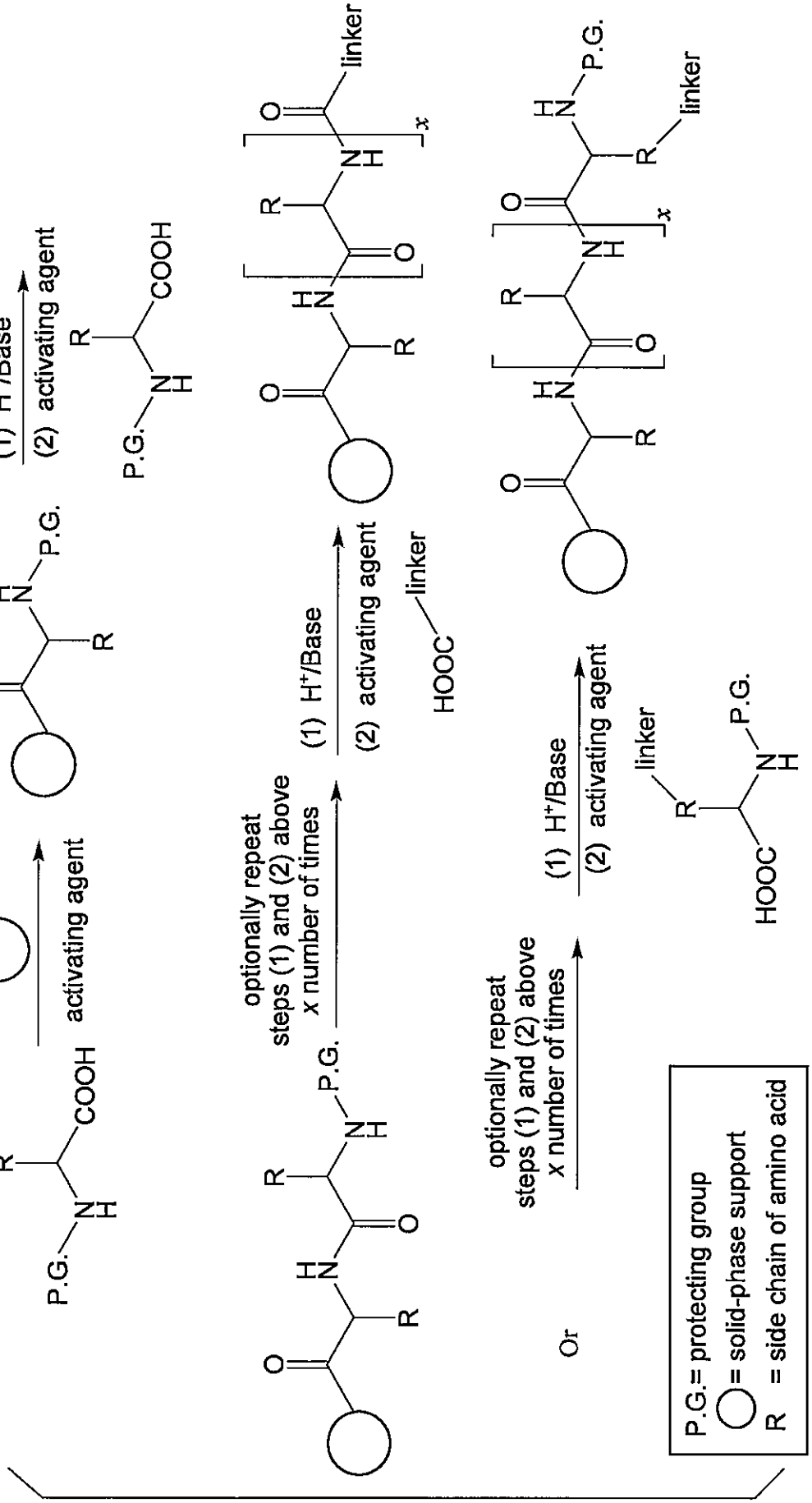

activating agent
(1) H+/Base
(2) activating agent
optionally repeat steps (1) and (2) above x number of times
(1) H+/Base
(2) activating agent
linker
HOOC
Or
optionally repeat steps (1) and (2) above x number of times
(1) H+/Base
(2) activating agent
linker
HOOC
P.G.= protecting group
= solid-phase support
R = side chain of amino acid

FIG. 2A

```
VL
                FR1                 CDR1              FR2         CDR2                    FR3                  CDR3       FR4
                                                                                                                  1
          1         2         3               4         5         6         7         8         9         0
12345678901234567890123 45678901abcde234 567890123456789 0123456 78901234567890123456789012345678 901234567 8901234567

m38C2 DVVMTQTPLSLPVRLGDQASISC RSSQSLLHTYGSPYLN WYLQKPGQSPKLLIY KVSNRFS GVPDRFSGSGSGTDFTLRISRVEAEDLGVYFC SQGTHLPYT FGGGTKLEIK
      ***   * *  ****  *** *                                  *            *  ****  **                     *
h38C2 ELQMTQSPSSLSASVGDRVTITC RSSQSLLHTYGSPYLN WYLQKPGQSPKLLIY KVSNRFS GVPSRFSGSGSGTDFTLTISSLQPEDFAVYFC SQGTHLPYT FGGGTKVEIK
      **                      *   ********      *    **       ** ***                          * *  * **** *

DPK-9 DIQMTQSPSSLSASVGDRVTITC RASQSISS-----YLN WYQQKPGKAPKLLIY AASSLQS GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC QQSYSTP
JK4                                                                                                    LT FGGGTKVEIK


VH
                FR1                 CDR1        FR2             CDR2                        FR3                          CDR3        FR4
                                                                                                                          1           1
          1         2         3               4         5         6         7         8         9         0           1
12345678901234567890123456789 0 1ab2345 67890123456789 012abc3456789012345 6789012345678901 2abc345678901234 56789012 34567890123
m38C2 EVKLVESGGGLVQPGGTMKLSCEISGLTFR N--YWMS WVRQSPEKGLEWVA EIRLRSDNYATHYAESVKG KFTISRDDSKSRLYLQMNSLRTEDTGIYYCKT YFY-SFSY WGQGTLVTVSA
   *          ***   ** * *                 *                  *    *  **       *                                    *
h38C2 EVQLVESGGGLVQPGGSLRLSCAASGFTFS N--YWMS WVRQSPEKGLEWVS EIRLRSDNYATHYAESVKG RFTISRDNSKNTLYLQMNSLRAEDTGIYYCKT YFY-SFSY WGQGTLVTVSS
     *                           * *  *       * *       * **  **** *  *                                  **   **    * *

DP-47 EVQLLESGGGLVQPGGSLRLSCAASGFTFS S--YAMS WVRQAPGKGLEWVS AISG--SGGSTYYADSVKG RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK
JH4                                                                                                    YFDY WGQGTLVTVSS
```

FIG. 2B

Light Chain (219 amino acids): SEQ ID NO:1

ELQMTQSPSSLSASVGDRVTITCRSSQSLLHTYGSPYLNWYLQKPGQSPKLLIYKVSN
RFSGVPSRFSGSGSGTDFTLTISSLQPEDFAVYFCSQGTHLPYTFGGGTKVEIKRTVAA
PSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSK
DSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Heavy chain (448 amino acids): SEQ ID NO:2

EVQLVESGGGLVQPGGSLRLSCAASGFTFSNYWMSWVRQSPEKGLEWVSEIRLRSD
NYATHYAESVKGRFTISRDNSKNTLYLQMNSLRAEDTGIYYC**K**TYFYSFSYWGQGT
LVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT
FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCP
PCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK
GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPV
LDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

FIG. 3A

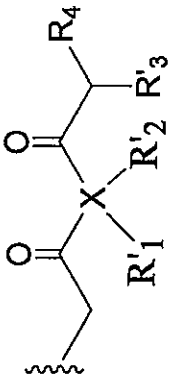


FIG. 3B

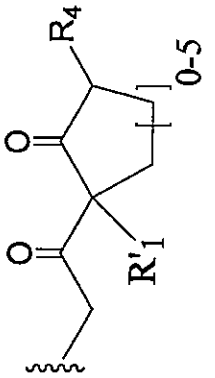


FIG. 3C

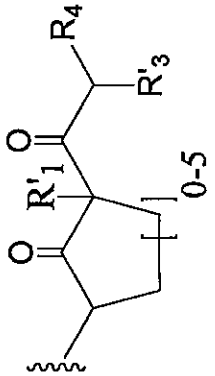


FIG. 3D

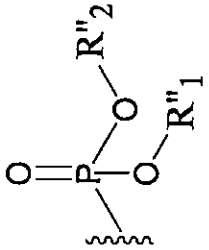


FIG. 3E

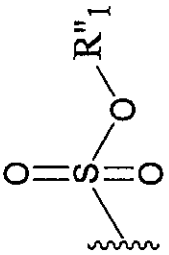


FIG. 3F

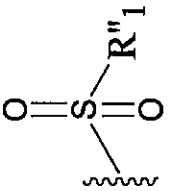


FIG. 3G

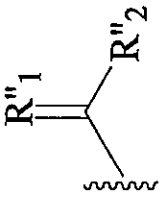


FIG. 4A

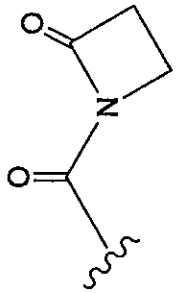


FIG. 4B

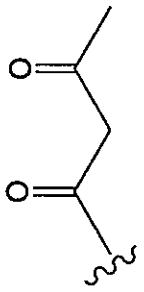


FIG. 4C

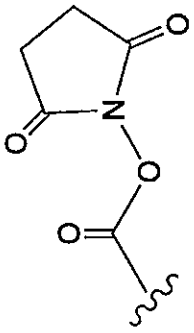


FIG. 4D

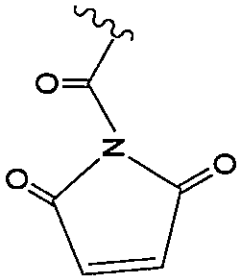


FIG. 4E

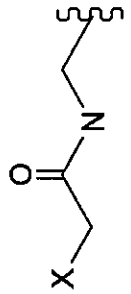


FIG. 4F

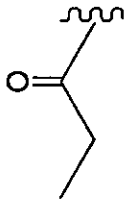


FIG. 4G

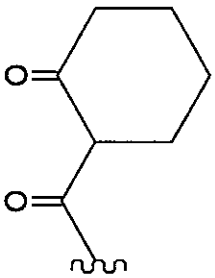


FIG. 4H

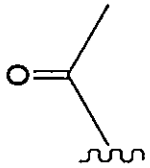


FIG. 5A

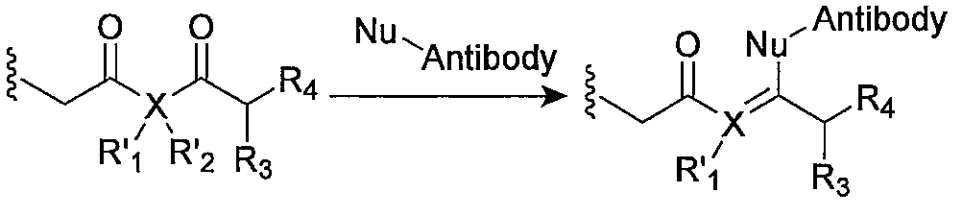


FIG. 5B

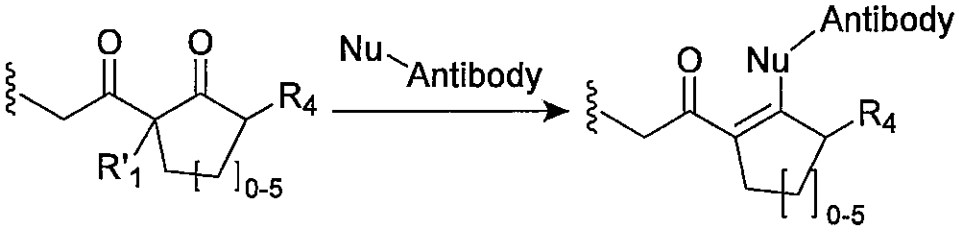


FIG. 5C

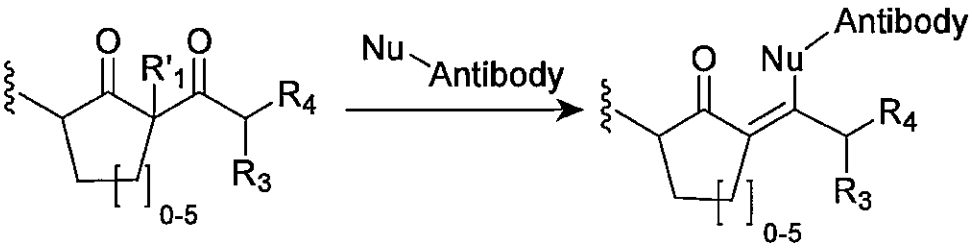


FIG. 5D

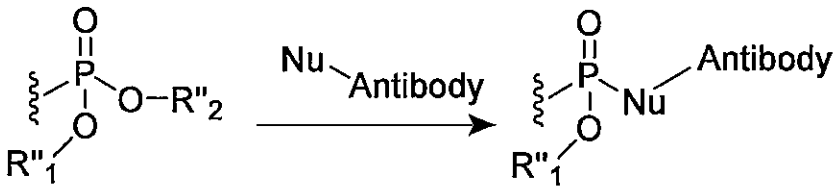


FIG. 5E

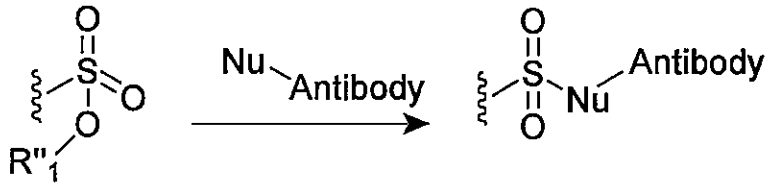


FIG. 5F

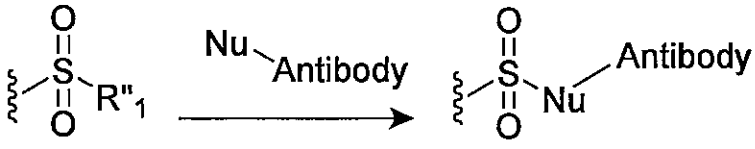


FIG. 5G

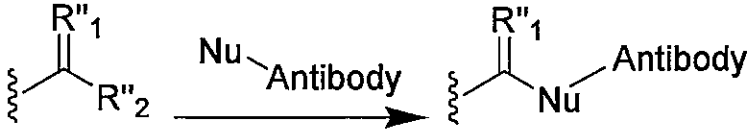


FIG. 6A

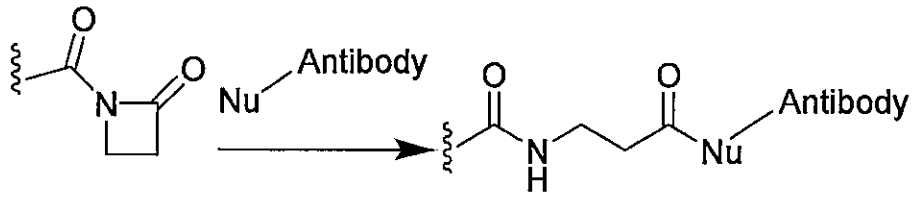


FIG. 6B

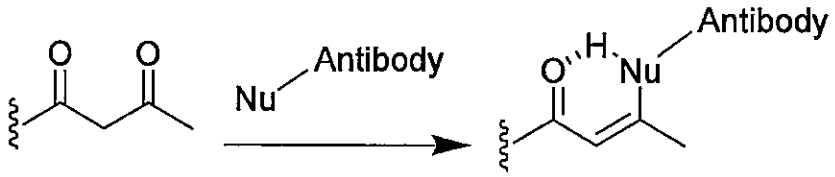


FIG. 6C

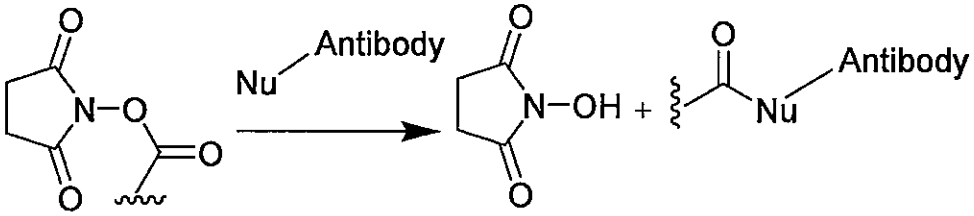


FIG. 6D

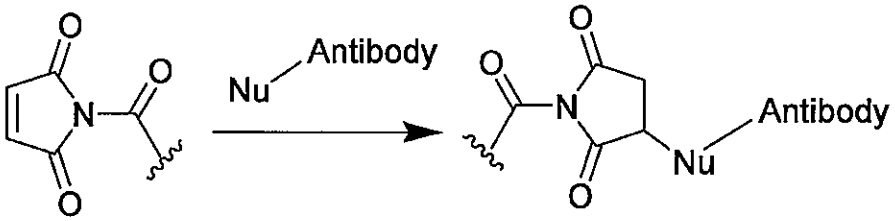


FIG. 6E

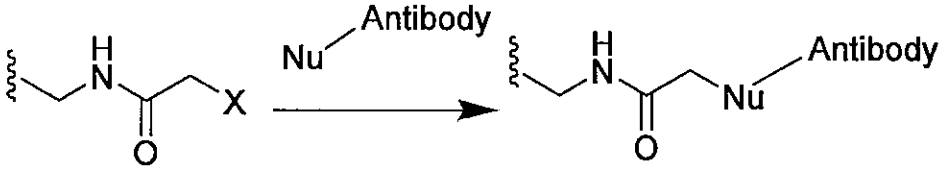


FIG. 6F

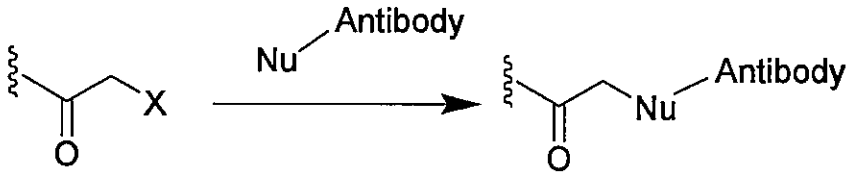


FIG. 6G

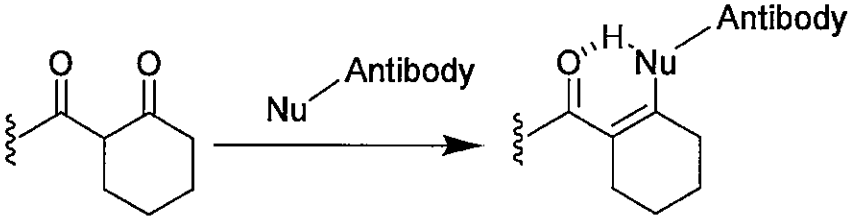


FIG. 6H

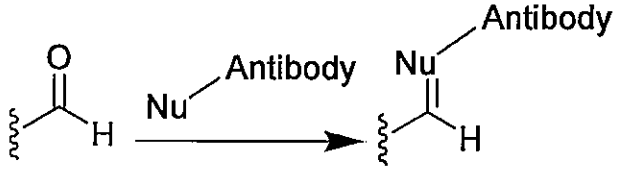


FIG. 7

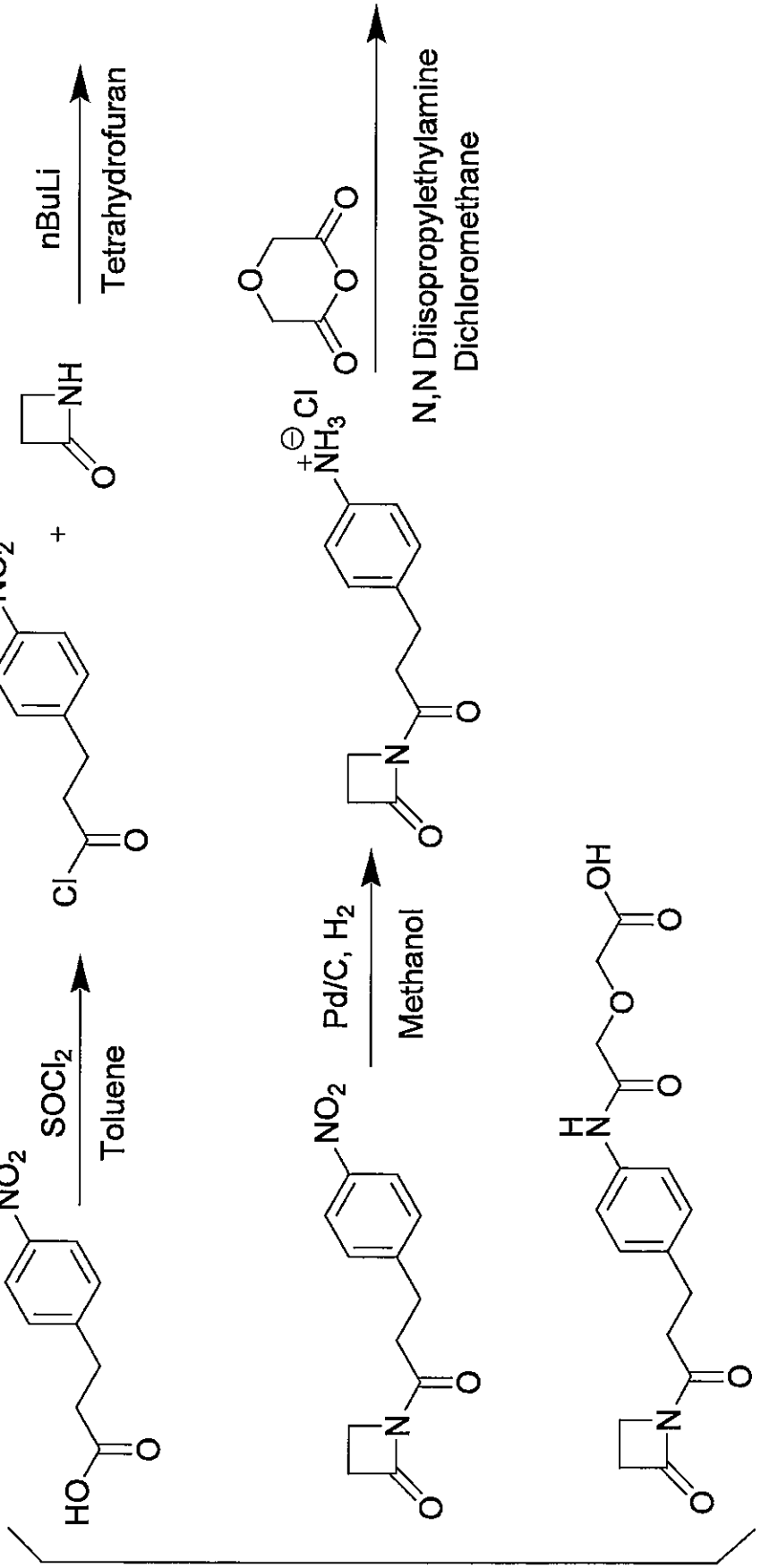
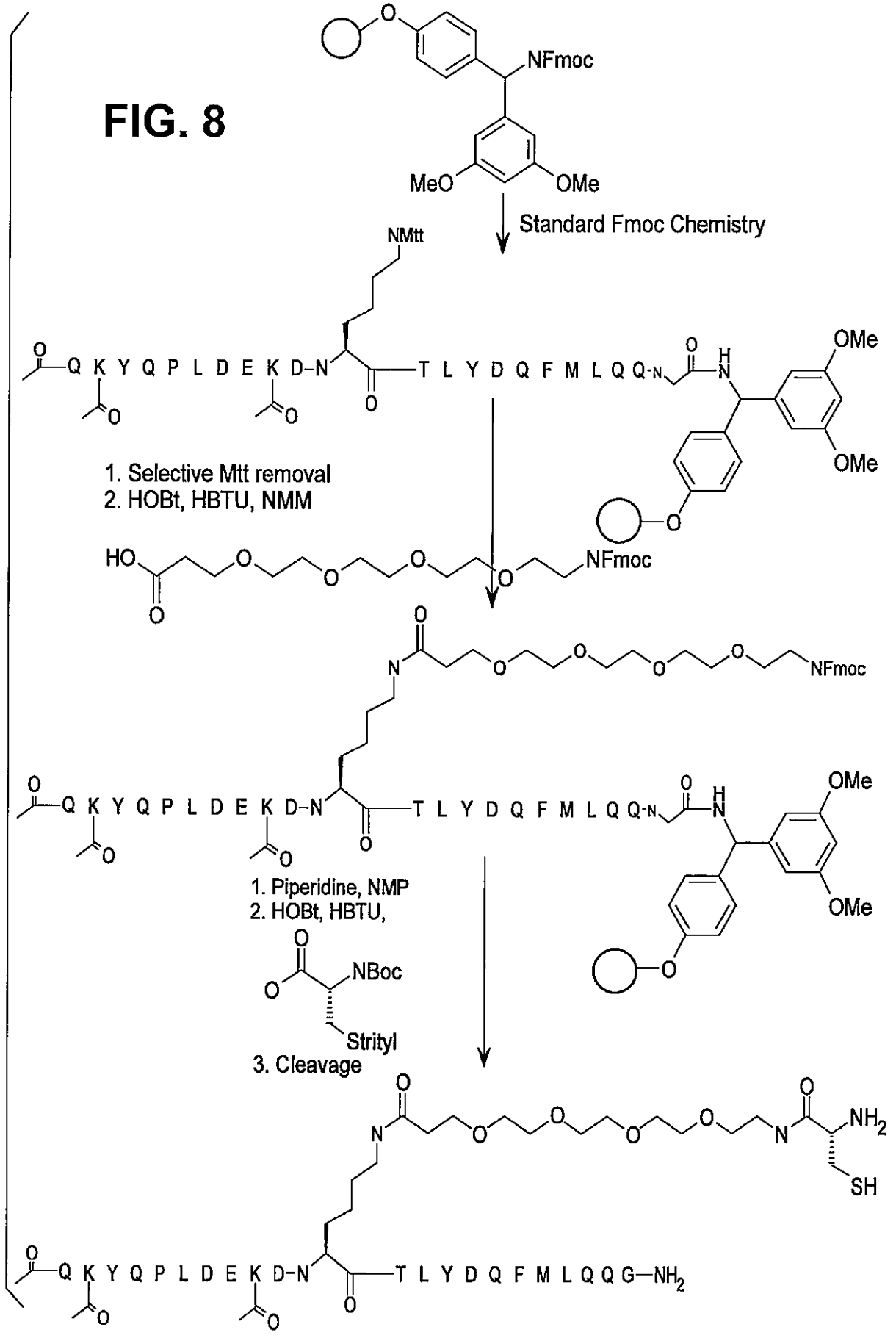

nBuLi
Tetrahydrofuran
NH
O
+
NO2
Cl
O
SOCl2
Toluene
HO
O
NO2
O
O
O
O
N,N Diisopropylethylamine
Dichloromethane
Cl
NH3
O
N
O
Pd/C, H2
Methanol
NO2
O
N
O
OH
O
O
O
HN
O
N
O

FIG. 8


NFmoc
MeO
OMe
Standard Fmoc Chemistry
NMtt
Q K Y Q P L D E K D-N
T L Y D Q F M L Q Q-N
H
OMe
OMe
1. Selective Mtt removal
2. HOBt, HBTU, NMM
HO
NFmoc
NFmoc
1. Piperidine, NMP
2. HOBt, HBTU,
NBoc
Strityl
3. Cleavage
NH2
SH
T L Y D Q F M L Q Q G—NH2

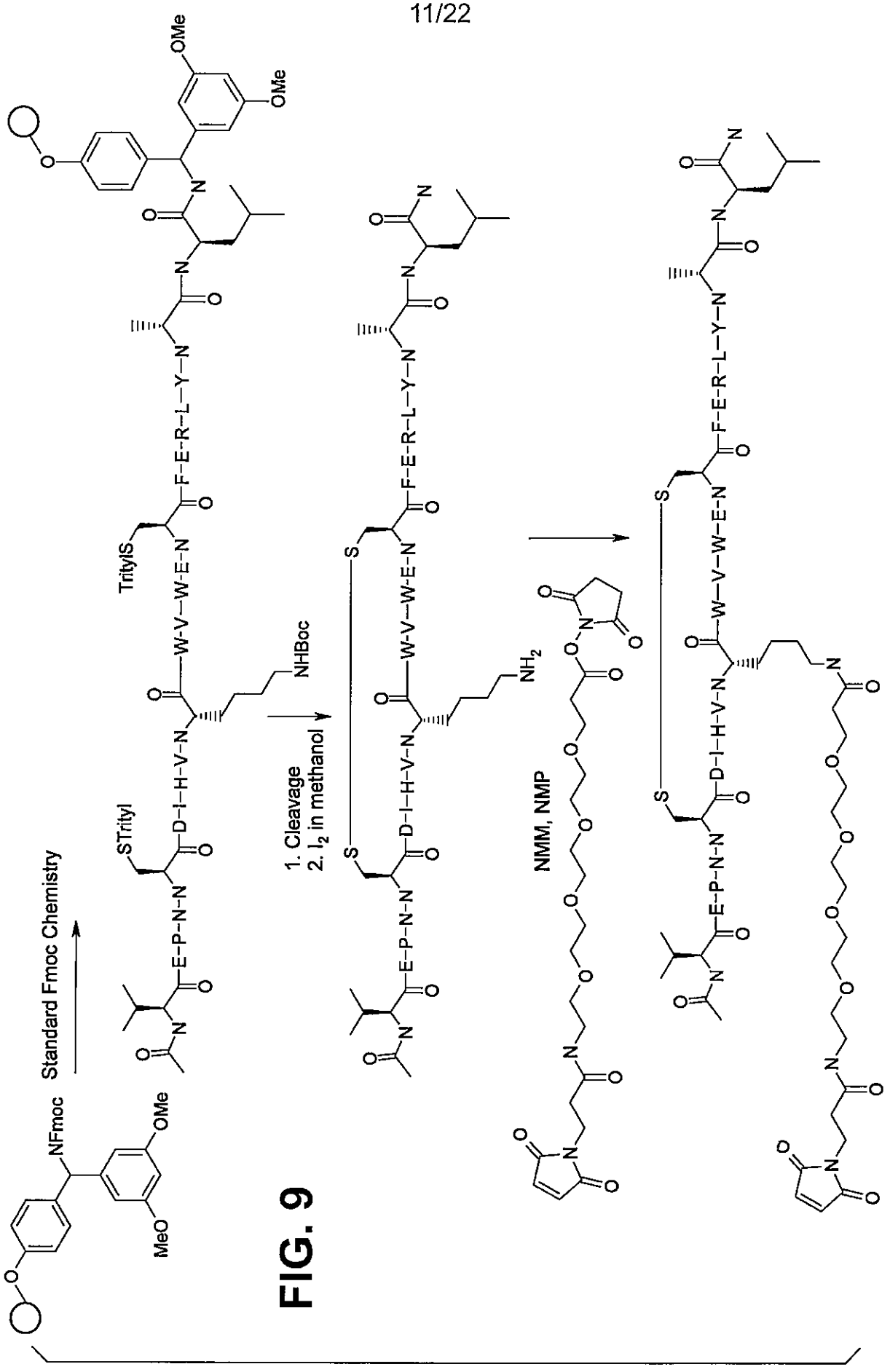

NFmoc
OMe
MeO
Standard Fmoc Chemistry
STrityl
E-P-N-N
D-I-H-V-N
W-V-W-E-N
TrityIS
F-E-R-L-Y-N
NHBoc
1. Cleavage
2. I_2 in methanol
NH_2
NMM, NMP

FIG. 9

FIG. 10

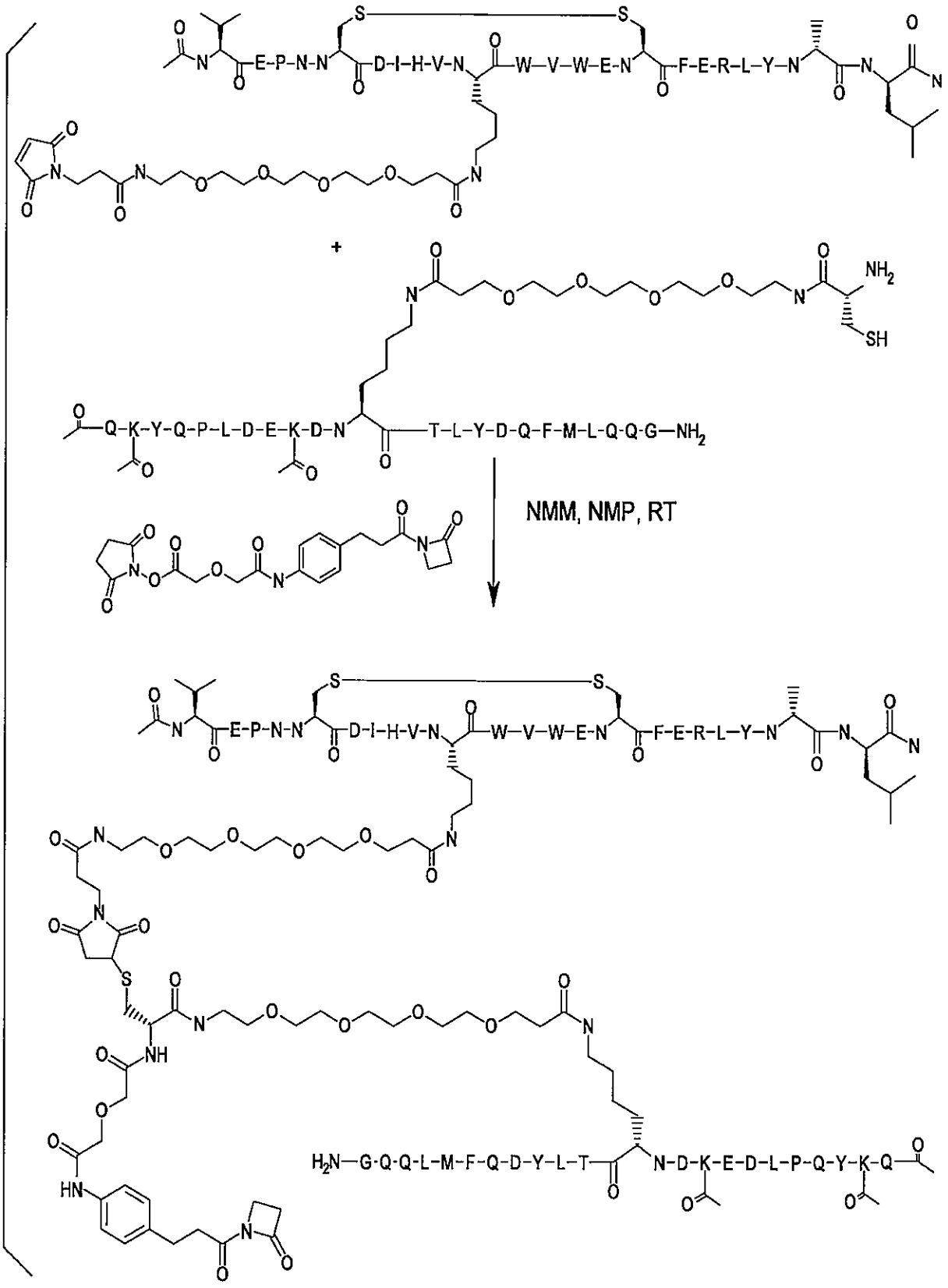

E-P-N-N
D-I-H-V-N
W-V-W-E-N
F-E-R-L-Y-N
Q-K-Y-Q-P-L-D-E-K-D-N
T-L-Y-D-Q-F-M-L-Q-Q-G—NH2
NH2
SH
NMM, NMP, RT
H2N—G-Q-Q-L-M-F-Q-D-Y-L-T
N-D-K-E-D-L-P-Q-Y-K-Q

FIG. 11

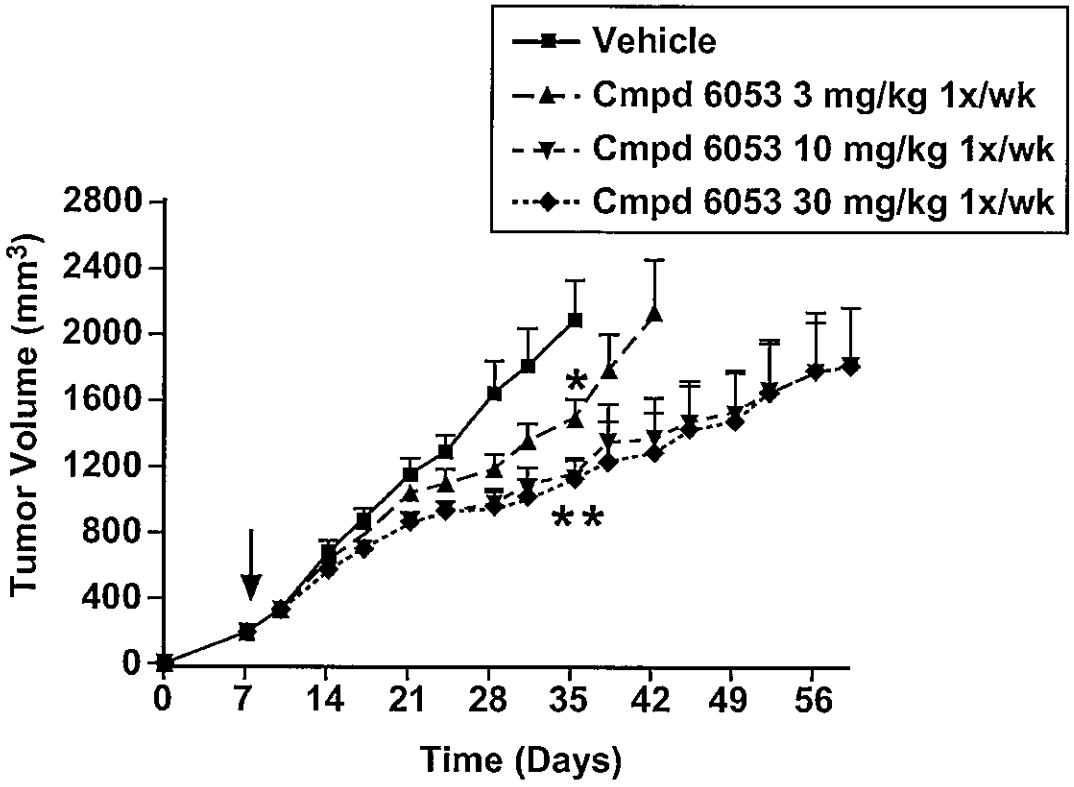

Vehicle
Cmpd 6053 3 mg/kg 1x/wk
Cmpd 6053 10 mg/kg 1x/wk
Cmpd 6053 30 mg/kg 1x/wk
Tumor Volume (mm3)
2800
2400
2000
1600
1200
800
400
0
0
7
14
21
28
35
42
49
56
Time (Days)
*
**

FIG. 12

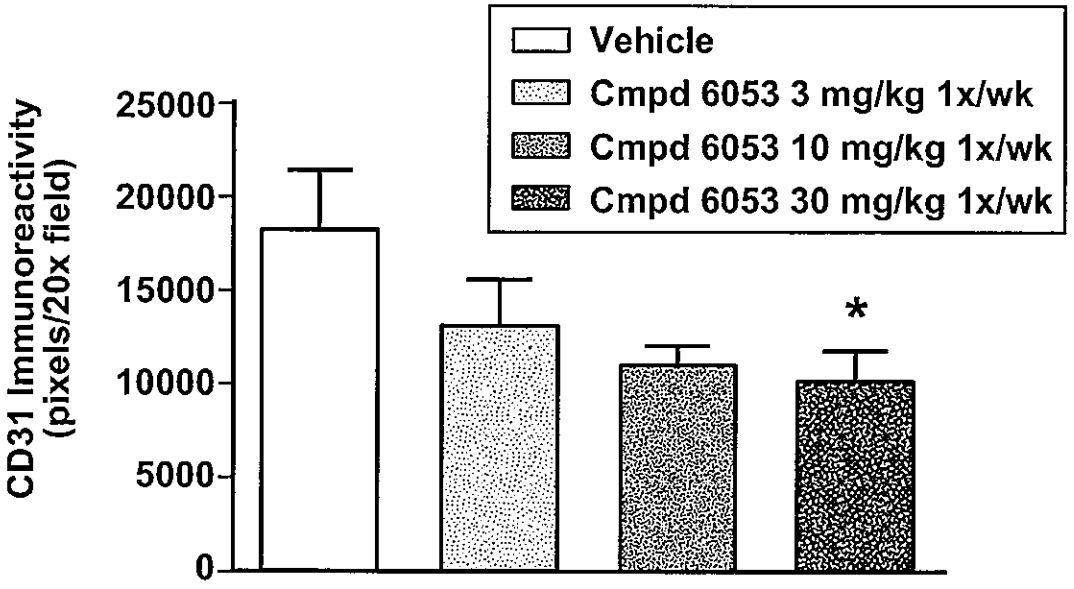

Vehicle
Cmpd 6053 3 mg/kg 1x/wk
Cmpd 6053 10 mg/kg 1x/wk
Cmpd 6053 30 mg/kg 1x/wk
CD31 Immunoreactivity (pixels/20x field)
25000
20000
15000
10000
5000
0
*

FIG. 13

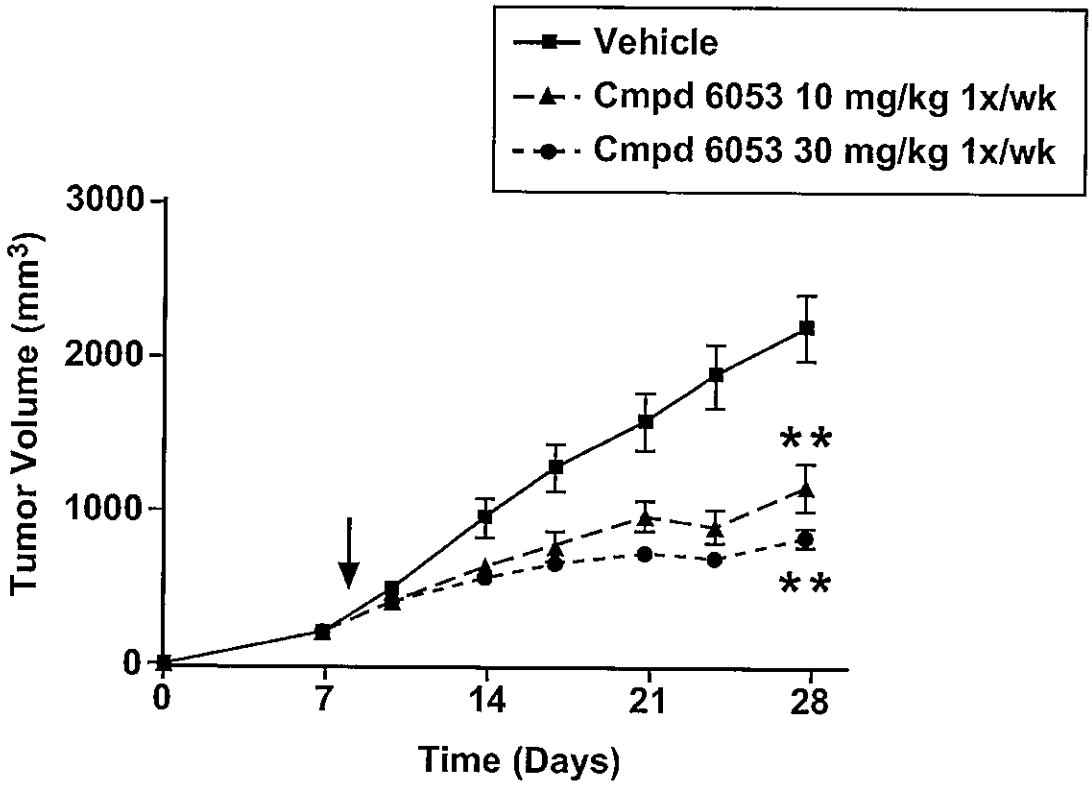

Vehicle
Cmpd 6053 10 mg/kg 1x/wk
Cmpd 6053 30 mg/kg 1x/wk
Tumor Volume (mm3)
3000
2000
1000
0
0
7
14
21
28
Time (Days)
**
**

FIG. 14

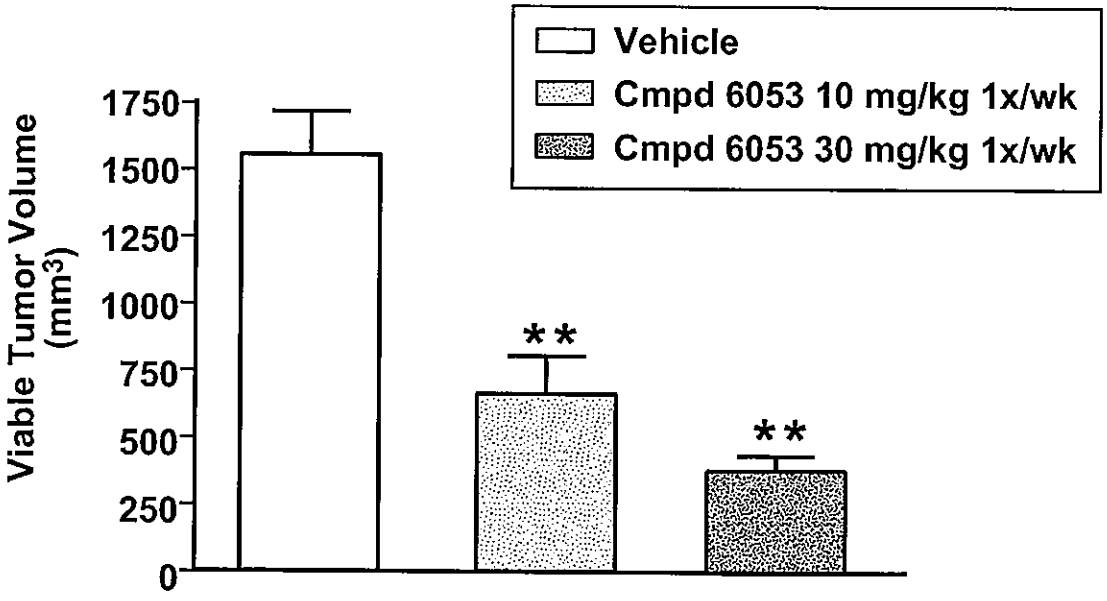

Vehicle
Cmpd 6053 10 mg/kg 1x/wk
Cmpd 6053 30 mg/kg 1x/wk
Viable Tumor Volume (mm3)
1750
1500
1250
1000
750
500
250
0
**
**

FIG.15

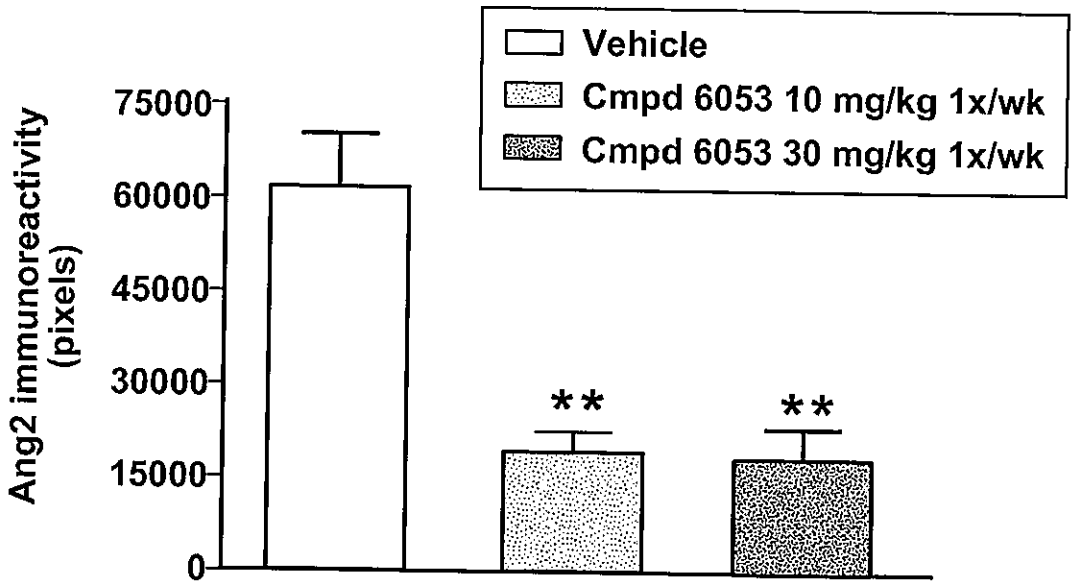

Vehicle
Cmpd 6053 10 mg/kg 1x/wk
Cmpd 6053 30 mg/kg 1x/wk
Ang2 immunoreactivity (pixels)
75000
60000
45000
30000
15000
0
**
**

FIG.16

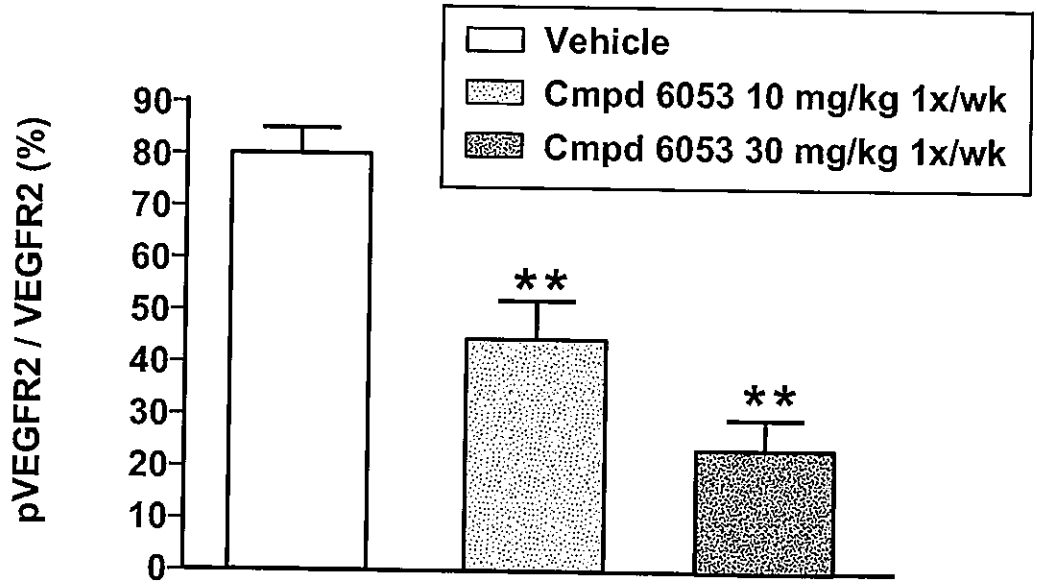

Vehicle
Cmpd 6053 10 mg/kg 1x/wk
Cmpd 6053 30 mg/kg 1x/wk
pVEGFR2 / VEGFR2 (%)
90
80
70
60
50
40
30
20
10
0
**
**

FIG. 17A

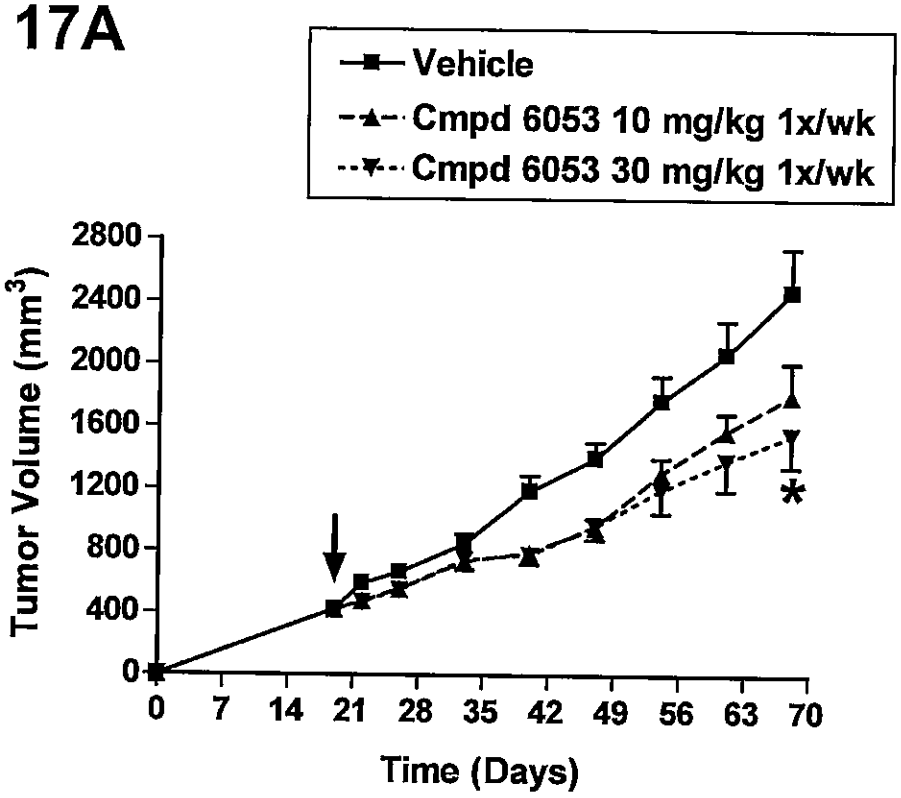


FIG. 17B

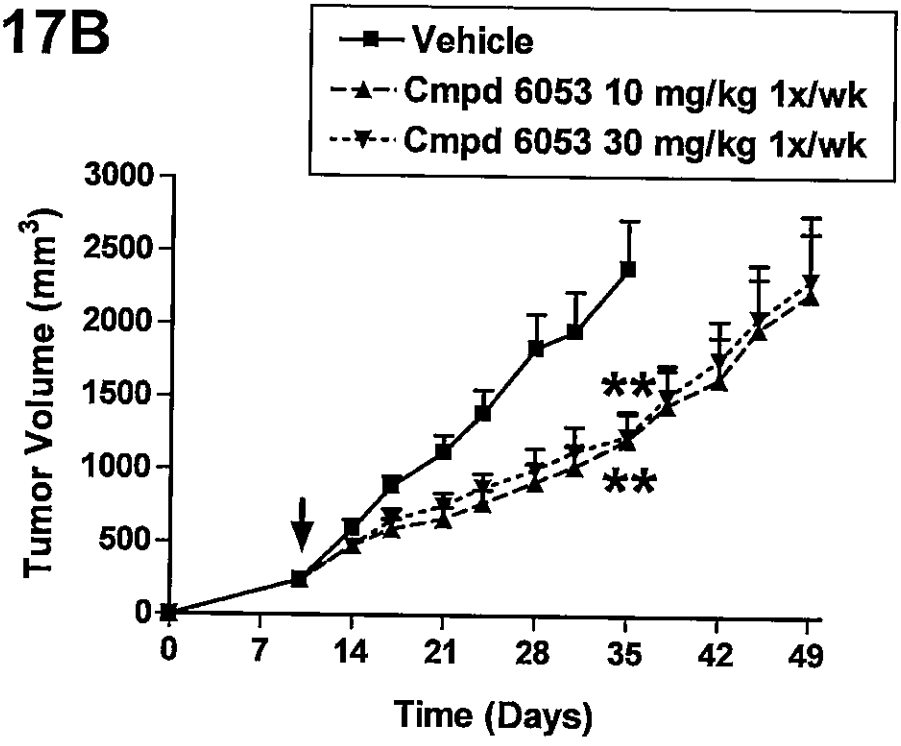


FIG. 18

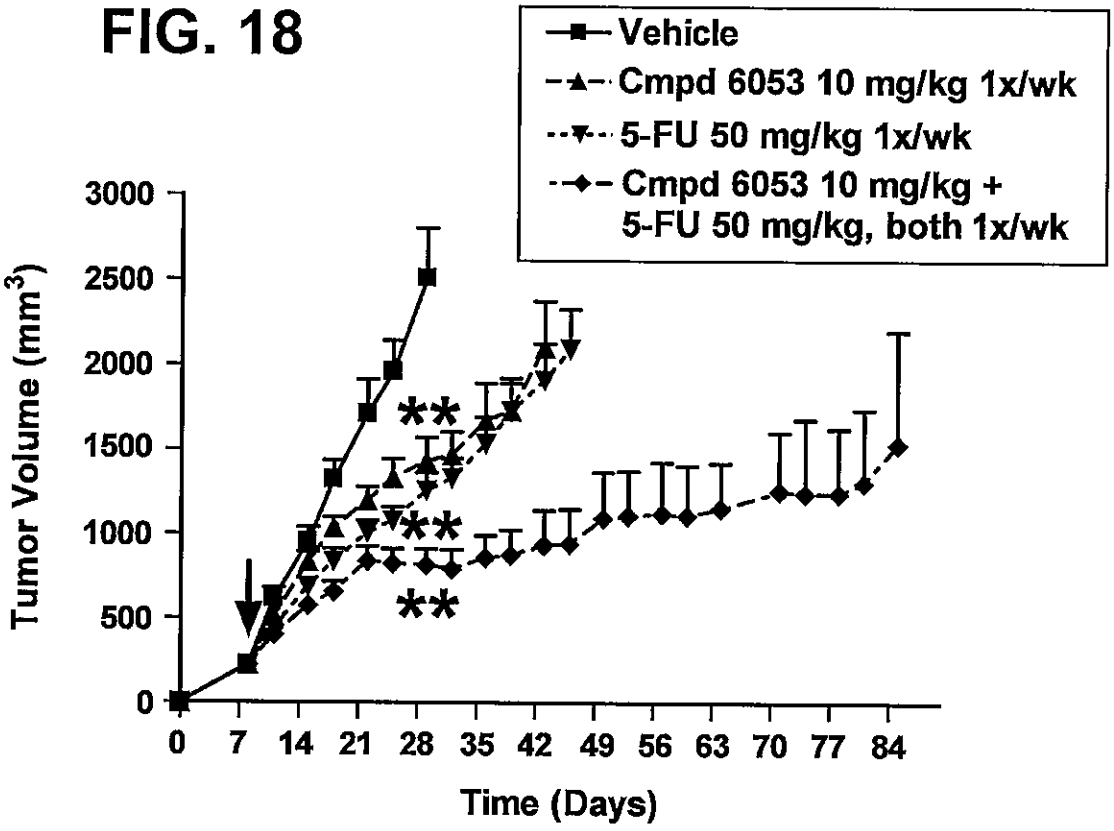

Vehicle
Cmpd 6053 10 mg/kg 1x/wk
5-FU 50 mg/kg 1x/wk
Cmpd 6053 10 mg/kg + 5-FU 50 mg/kg, both 1x/wk
Tumor Volume (mm3)
3000
2500
2000
1500
1000
500
0
0 7 14 21 28 35 42 49 56 63 70 77 84
Time (Days)

FIG. 19

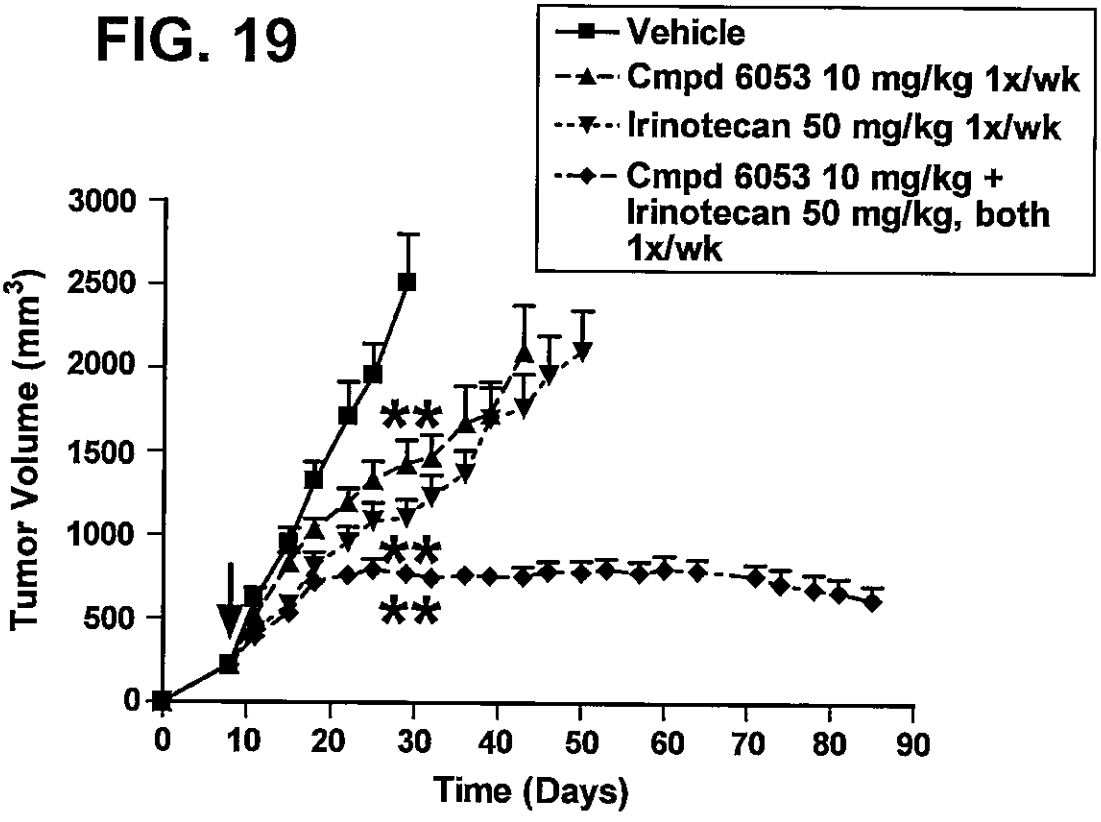

Vehicle
Cmpd 6053 10 mg/kg 1x/wk
Irinotecan 50 mg/kg 1x/wk
Cmpd 6053 10 mg/kg + Irinotecan 50 mg/kg, both 1x/wk
Tumor Volume (mm3)
3000
2500
2000
1500
1000
500
0
0 10 20 30 40 50 60 70 80 90
Time (Days)

FIG. 20

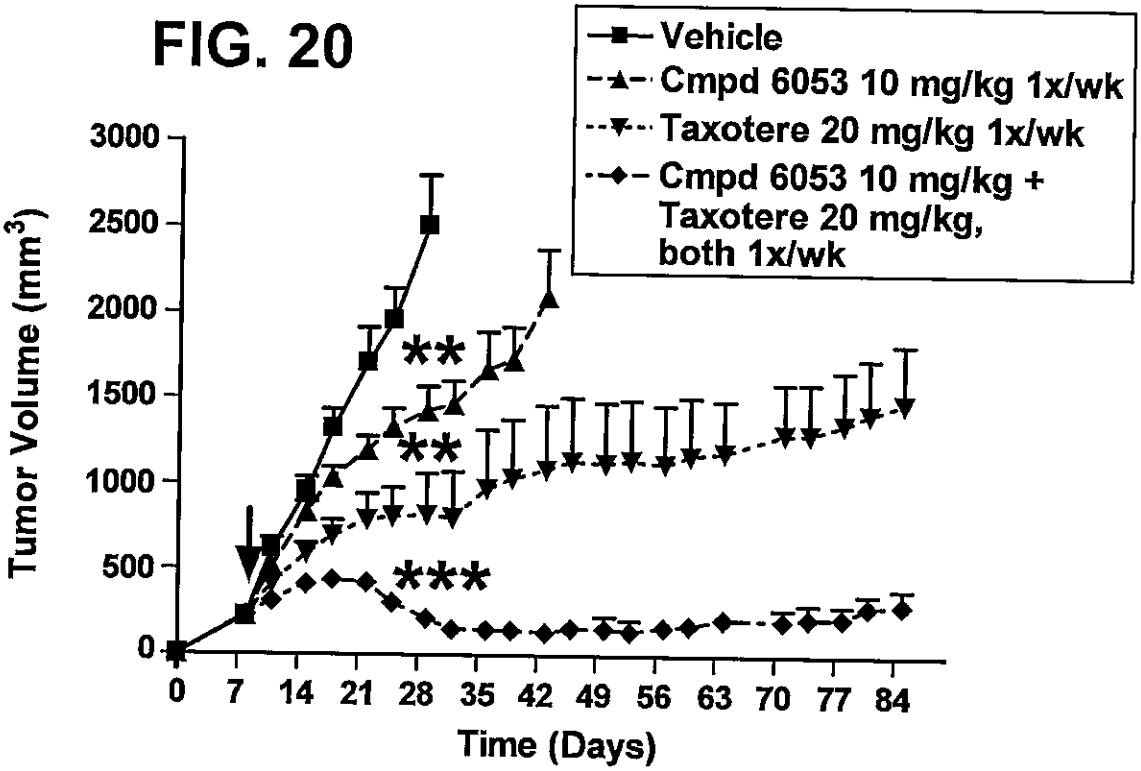

Vehicle
Cmpd 6053 10 mg/kg 1x/wk
Taxotere 20 mg/kg 1x/wk
Cmpd 6053 10 mg/kg + Taxotere 20 mg/kg, both 1x/wk
Tumor Volume (mm3)
3000
2500
2000
1500
1000
500
0
0 7 14 21 28 35 42 49 56 63 70 77 84
Time (Days)
**
**
***

FIG. 21

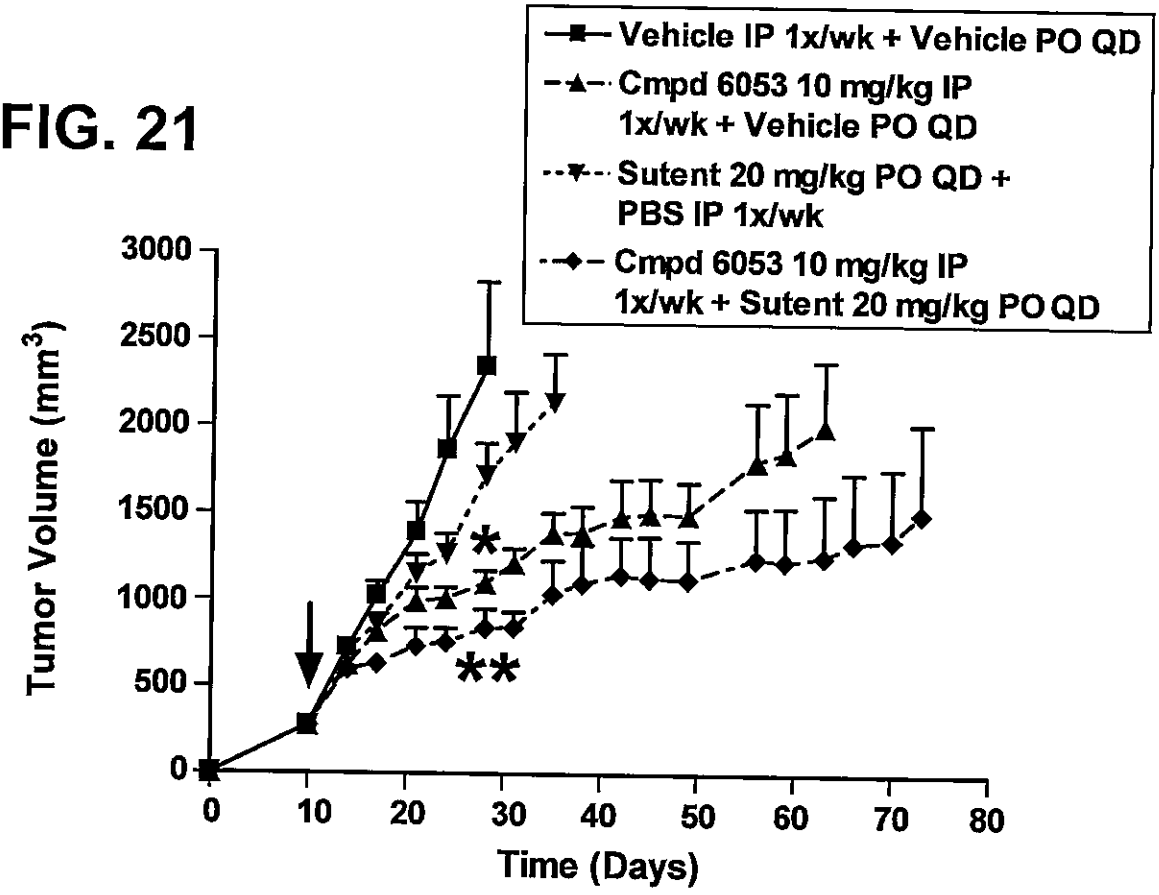

Vehicle IP 1x/wk + Vehicle PO QD
Cmpd 6053 10 mg/kg IP 1x/wk + Vehicle PO QD
Sutent 20 mg/kg PO QD + PBS IP 1x/wk
Cmpd 6053 10 mg/kg IP 1x/wk + Sutent 20 mg/kg PO QD
Tumor Volume (mm3)
3000
2500
2000
1500
1000
500
0
0 10 20 30 40 50 60 70 80
Time (Days)
*
**

FIG. 22

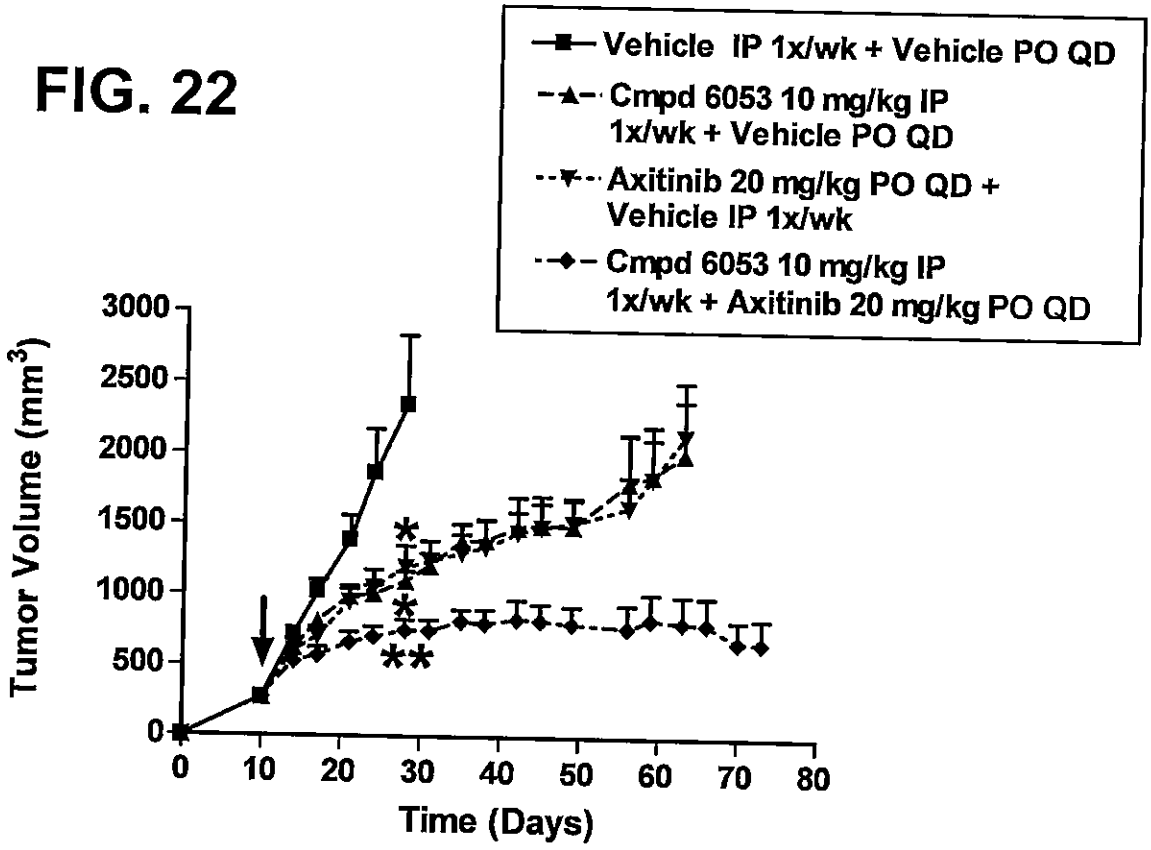

Vehicle IP 1x/wk + Vehicle PO QD
Cmpd 6053 10 mg/kg IP 1x/wk + Vehicle PO QD
Axitinib 20 mg/kg PO QD + Vehicle IP 1x/wk
Cmpd 6053 10 mg/kg IP 1x/wk + Axitinib 20 mg/kg PO QD
Tumor Volume (mm3)
3000
2500
2000
1500
1000
500
0
0
10
20
30
40
50
60
70
80
Time (Days)

FIG. 23

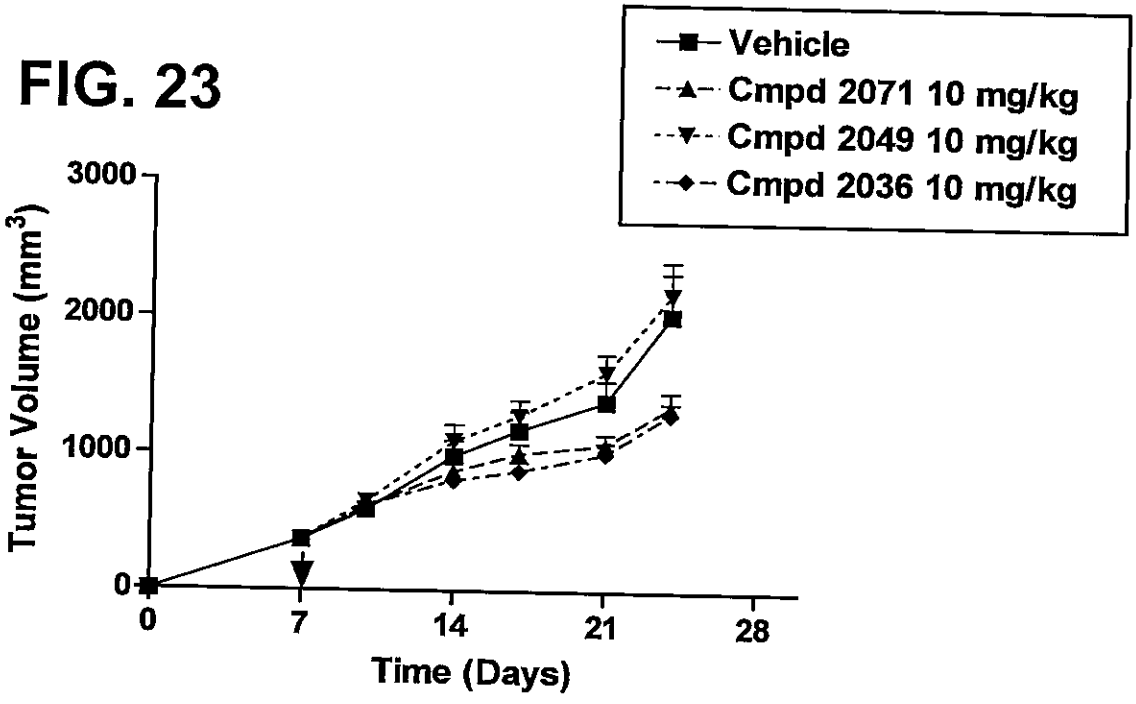

Vehicle
Cmpd 2071 10 mg/kg
Cmpd 2049 10 mg/kg
Cmpd 2036 10 mg/kg
Tumor Volume (mm3)
3000
2000
1000
0
0
7
14
21
28
Time (Days)

FIG. 24

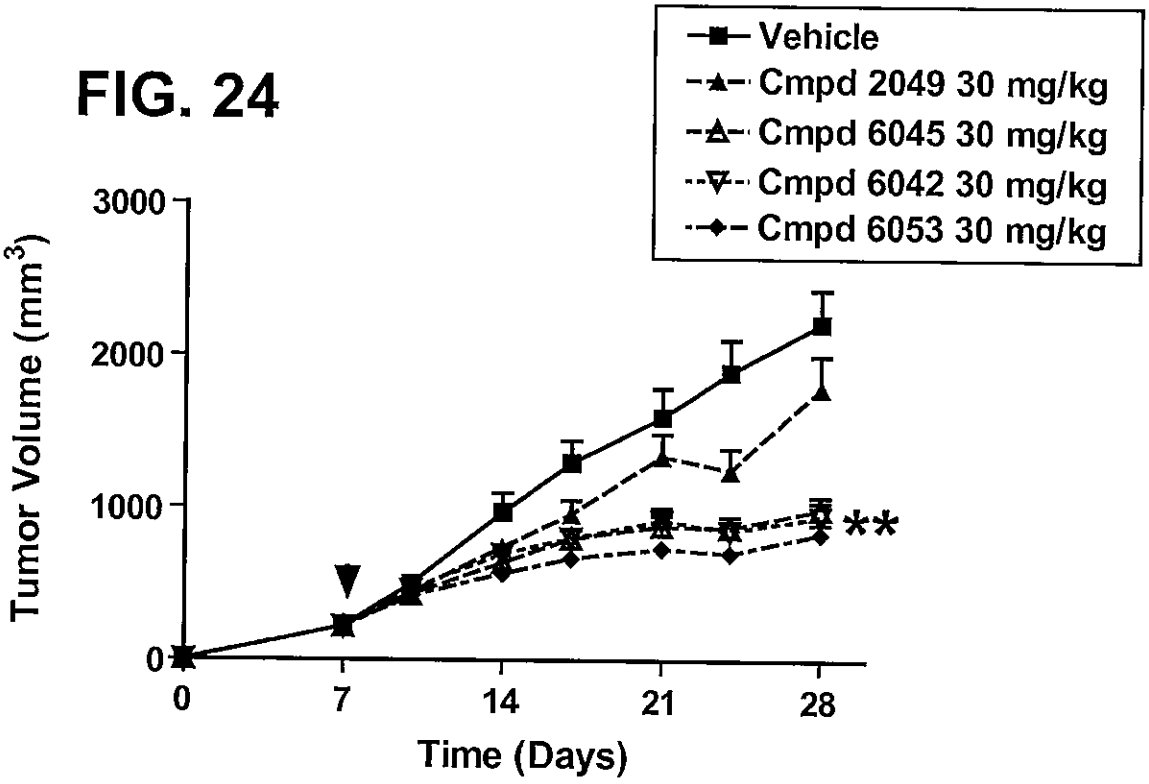

Vehicle
Cmpd 2049 30 mg/kg
Cmpd 6045 30 mg/kg
Cmpd 6042 30 mg/kg
Cmpd 6053 30 mg/kg
Tumor Volume (mm3)
3000
2000
1000
0
0
7
14
21
28
Time (Days)
**

FIG. 25

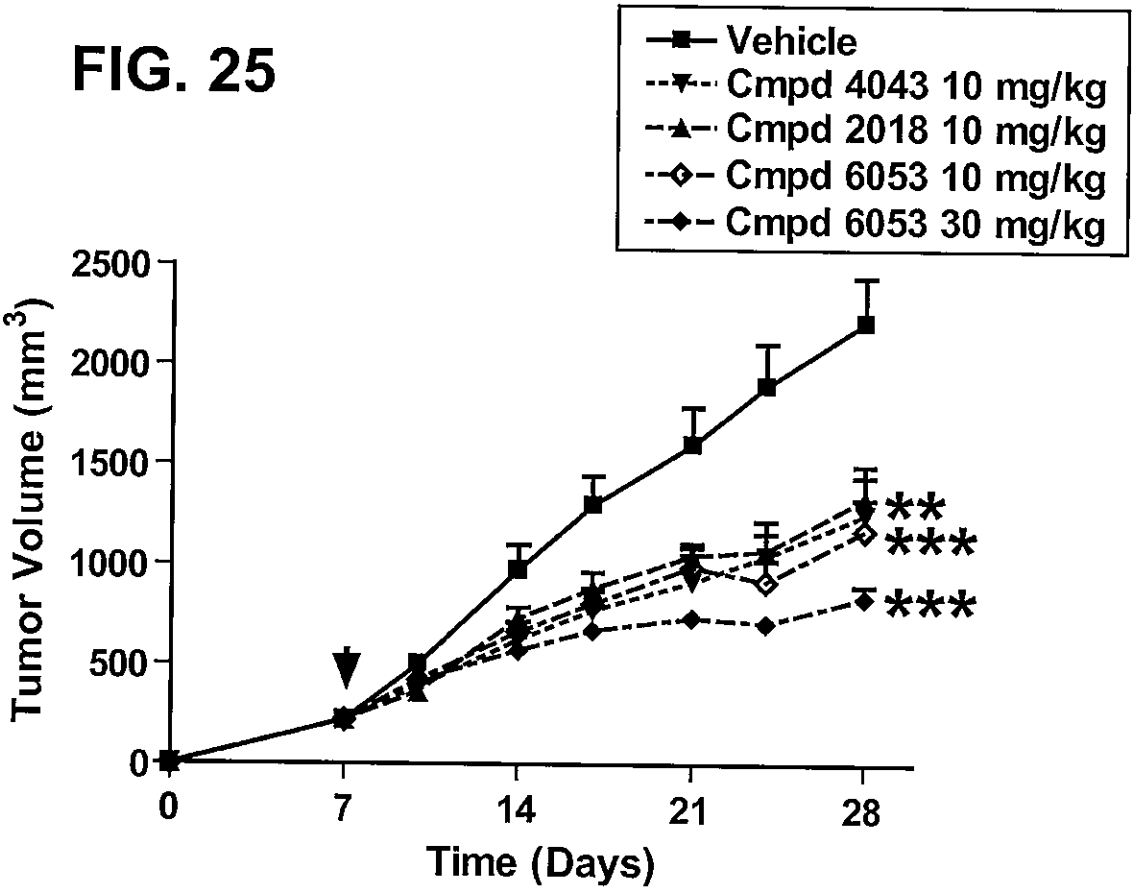

Vehicle
Cmpd 4043 10 mg/kg
Cmpd 2018 10 mg/kg
Cmpd 6053 10 mg/kg
Cmpd 6053 30 mg/kg
Tumor Volume (mm3)
2500
2000
1500
1000
500
0
0
7
14
21
28
Time (Days)
**
***
***

FIG. 26

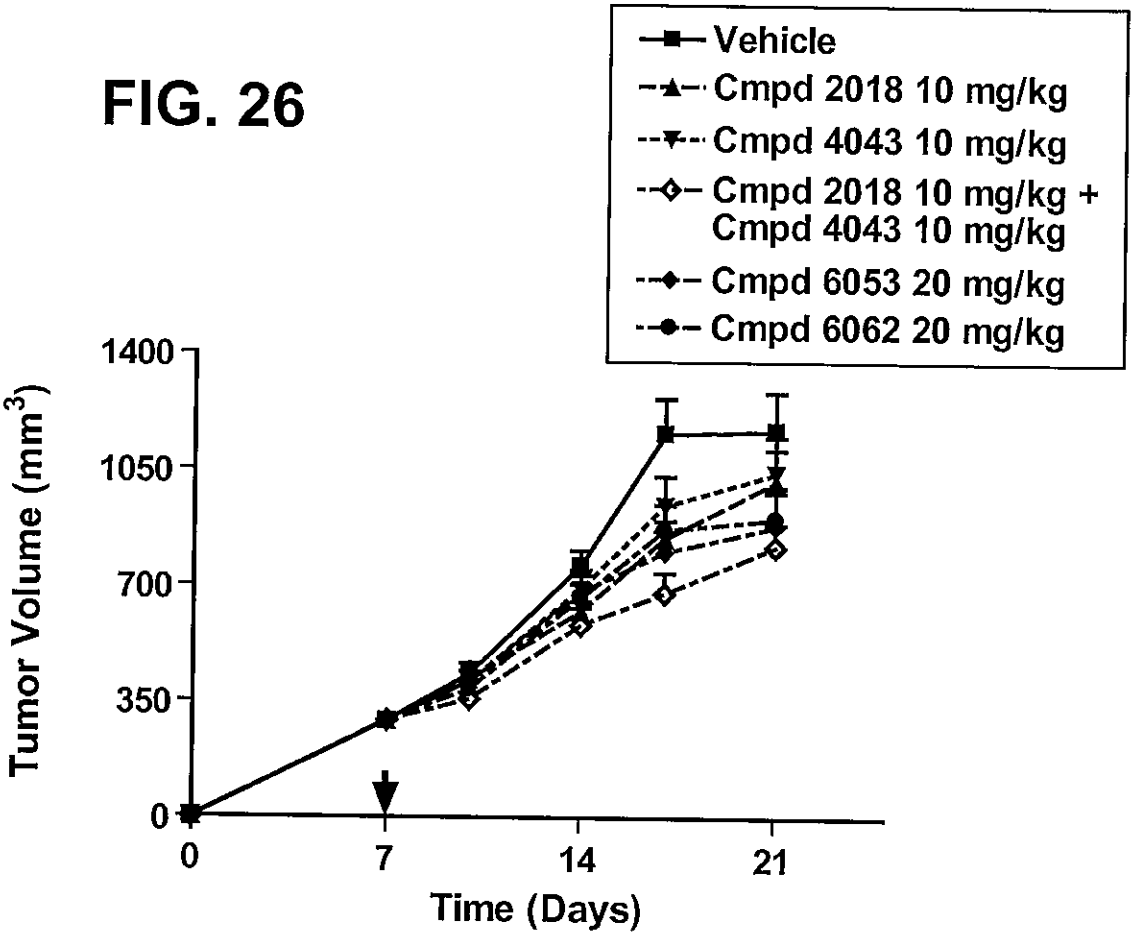

Vehicle
Cmpd 2018 10 mg/kg
Cmpd 4043 10 mg/kg
Cmpd 2018 10 mg/kg + Cmpd 4043 10 mg/kg
Cmpd 6053 20 mg/kg
Cmpd 6062 20 mg/kg
Tumor Volume (mm3)
1400
1050
700
350
0
0
7
14
21
Time (Days)

FIG. 27

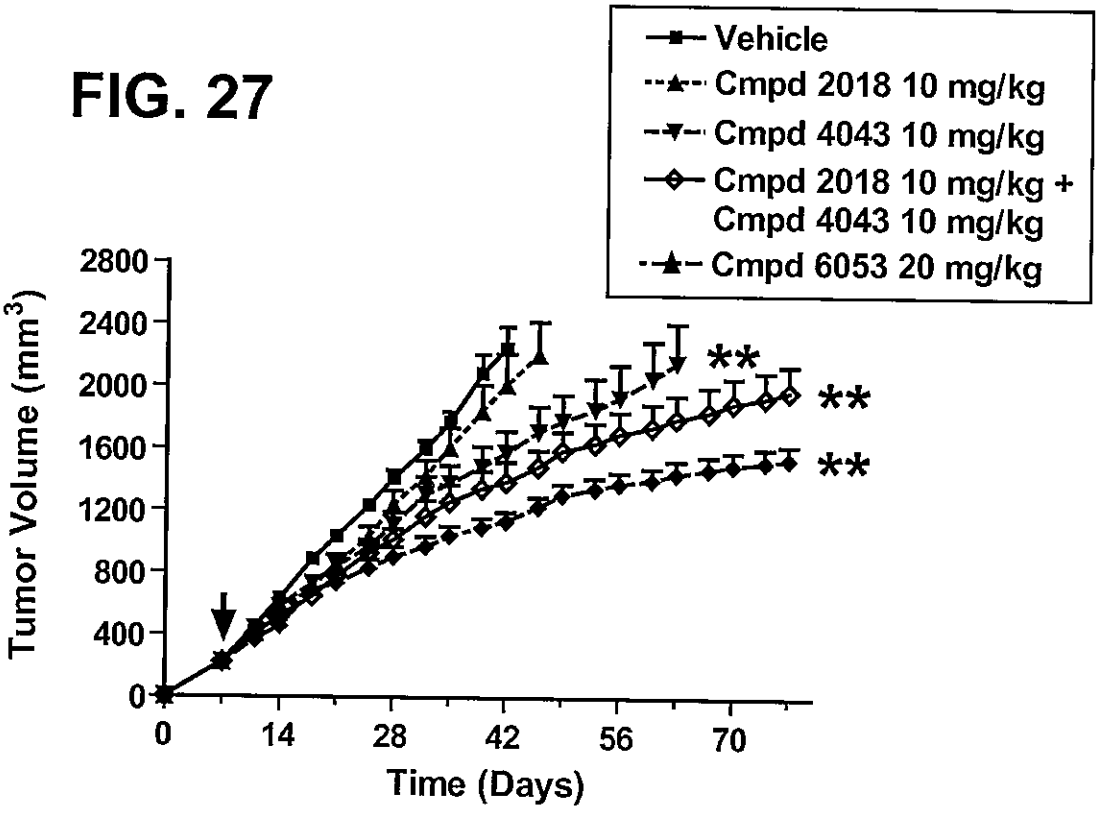

Vehicle
Cmpd 2018 10 mg/kg
Cmpd 4043 10 mg/kg
Cmpd 2018 10 mg/kg + Cmpd 4043 10 mg/kg
Cmpd 6053 20 mg/kg
Tumor Volume (mm3)
2800
2400
2000
1600
1200
800
400
0
0
14
28
42
56
70
Time (Days)
**
**
**

FIG. 28

FIGURE 28

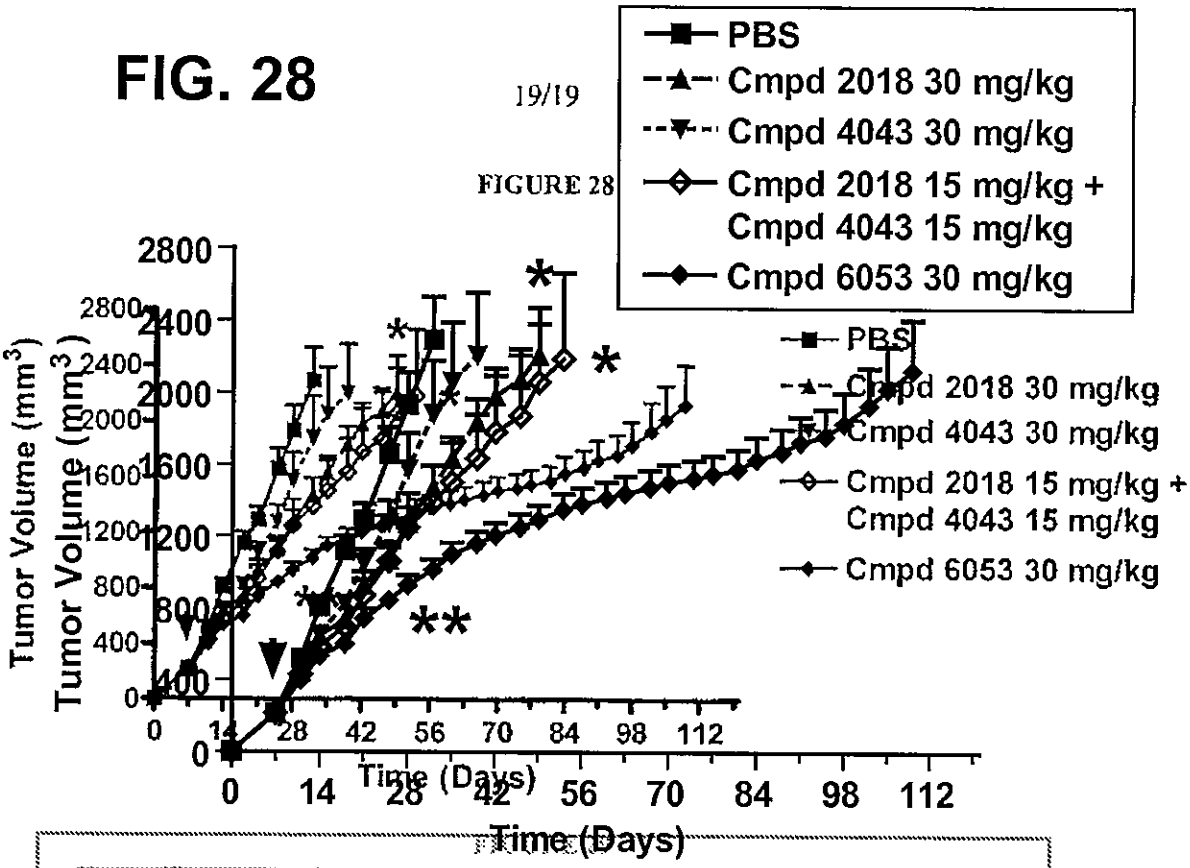


FIG. 29

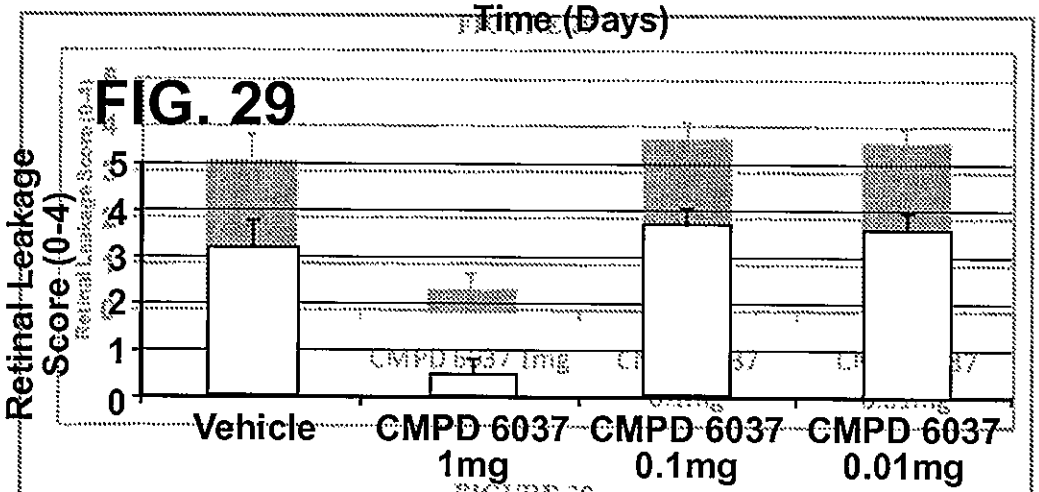


FIGURE 30

FIG. 30

